

2/3/05

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NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

| | |
|------------|---|
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STRUCTURE FILE UPDATES: 30 JAN 2005 HIGHEST RN 823177-37-3
DICTIONARY FILE UPDATES: 30 JAN 2005 HIGHEST RN 823177-37-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

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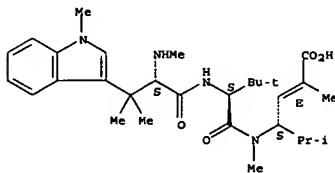
=> s hemiasterlin/cn
L1 1 HEMIASTERLIN/CN

=> d

2/3/05

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 157207-90-4 RDBISTRY
CN L-Valinamide, N, β , β ,1-tetramethyl-L-tryptophyl-N-[(1S,2R)-3-carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Valinamide, N, β , β ,1-tetramethyl-L-tryptophyl-N-[3-carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl-, (S-(8))-
OTHER NAMES:
CN (-)-Hemiamsterlin
CN Hemiassterlin
CN Milnamide B
PS STEREOSEARCH
MF C30 H46 N4 O4
SR CA
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
DT.CA Caplus document type: Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

31 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
31 REFERENCES IN FILE CAPLUS (1907 TO DATE)

10667864

2/3/05

=> logoff y
COST IN U.S. DOLLARS

FULL ESTIMATED COST

| | |
|---------------------|------------------|
| SINCE FILE
ENTRY | TOTAL
SESSION |
| 6.87 | 7.08 |

STN INTERNATIONAL LOGOFF AT 11:34:47 ON 31 JAN 2005

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NEWS 12 DEC 17 CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS 13 DEC 17 THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
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NEWS 17 JAN 26 CA/CAPLUS - Expanded patent coverage to include the Russian Agency for Patents and Trademarks (ROSPATENT)

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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FILE 'HOME' ENTERED AT 11:18:14 ON 03 FEB 2005

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STRUCTURE FILE UPDATES: 1 FEB 2005 HIGHEST RN 824390-04-7
DICTIONARY FILE UPDATES: 1 FEB 2005 HIGHEST RN 824390-04-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

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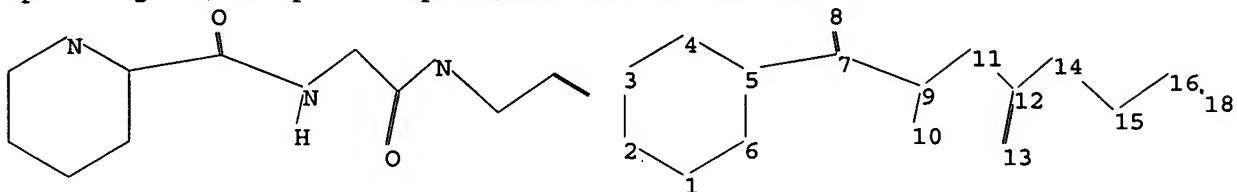
Crossover limits have been increased. See **HELP CROSSOVER** for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

\Rightarrow

2/3/05

Uploading C:\Stnexp4 corrupted\QUERIES\10667864.str



chain nodes :

7 8 9 10 11 12 13 14 15 16 18

ring nodes :

1 2 3 4 5 6

chain bonds :

5-7 7-8 7-9 9-10 9-11 11-12 12-13 12-14 14-15 15-16 16-18

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6

exact/norm bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-9 9-11 12-13 12-14 14-15

exact bonds :

5-7 9-10 11-12 15-16 16-18

isolated ring systems :

containing 1 :

Match level :

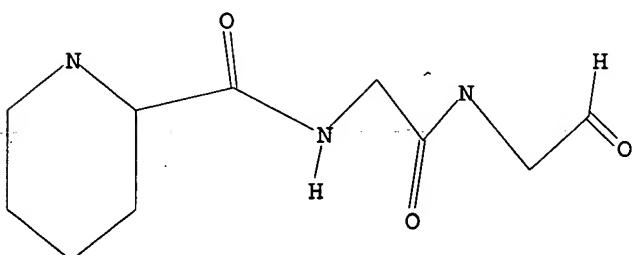
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 18:CLASS

L1 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 11

SAMPLE SEARCH INITIATED 11:18:54 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 18597 TO ITERATE

10667864

2/3/05

5.4% PROCESSED 1000 ITERATIONS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

0 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 363777 TO 380103
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s 11 ful
FULL SEARCH INITIATED 11:18:59 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 370581 TO ITERATE

100.0% PROCESSED 370581 ITERATIONS
SEARCH TIME: 00.00.05

9 ANSWERS

L3 9 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS
FULL ESTIMATED COST

| | SINCE FILE ENTRY | TOTAL SESSION |
|--|------------------|---------------|
| | 161.33 | 161.54 |

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FILE COVERS 1907 - 3 Feb 2005 VOL 142 ISS 6
FILE LAST UPDATED: 2 Feb 2005 (20050202/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

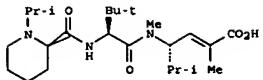
=> s 13
L4 6 L3

=> d abs fbib hitstr 1-6

10667864

2/3/05

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
GI



AB The invention provides compds. R1R2N(CR3R4)n-X1-NR5CHR6CONR7-R-X2-Q [R is an aliphatic, alicyclic, heteroaliph., heterocyclic, aryl or heteroaryl moiety; n is 0-4; X1, X2 are CRARB, CO, or SO2, where RA, RB are H or R; R1, R2 are H, OH, CORC or R, where RC is H, OH, CORD, or R and RD is R; R3, R4 are H or R; R5, R6, R7 are H, CORB or R, where RE is H, OH, ORF, or R and RF is a group defined by R; R7 may be absent when NR7 is linked to R via a double bond; two R1-R4 or two R5-R7 taken together may form a (hetero)alicyclic, (hetero)alicyclic(aryl), or (hetero)aryl moiety; Q is ORQ', SRQ', NRQ'RO'', N3, NOH, or R, where RQ' and RO'' are H or R or may combine as for R1-R4 or R5-R7 (with provisos) or their pharmaceutically-acceptable derive. for use in the treatment of cancer. Compds. of the invention, e.g., hemisterlin derivative I, were prepared and assayed for inhibition of cell growth. Active compds. were evaluated in the reversibility, MDR, mouse serum stability, and other assays.

AN 2004:999664 CAPLUS

DN 141:395816

TI Preparation of hemisterlin derivatives as antitumor agents
IN Kowalczyk, James J.; Kuznetsov, Galina; Schiller, Shawn; Seletsky, Boris M.; Spyvee, Mark; Yang, Hu

PA USA

SO U.S. Pat. Appl. Publ., 237 pp., Cont.-in-part of Appl. No.

PCT/US03/08888

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------|------|----------|-----------------|-------------|
| PI US 2004229819 | A1 | 20041118 | US 2003-667864 | 20030922 |
| | | | US 2002-366592P | P 20020322 |
| | | | WO 2003-US8888 | A2 20030321 |
| WO 2003082268 | A2 | 20031009 | WO 2003-US8888 | 20030321 |
| WO 2003082268 | A3 | 20040923 | | |

W: AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KB, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TO, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

AB Synthesis of title compds., e.g., (I), and preparation of reactants for these syntheses, for use in the treatment of autoimmune disease or tumors via their cytostatic effect (no date) was claimed. Thus, N-methyl-B-DL-valinolyl tert-butylidiphenylsilylether (II) was prepared in three steps from methylamine, isobutyraldehyde, and malonic acid.

D-N-methyl-homo-prolyl-L-isoleucine (III) was also prepared in four steps from D-N-Boc-homoproline and L-isoleucine benzyl ester. II and III were coupled, the silyl protecting group removed, and the resulting alc. subjected to Swern oxidation to give an aldehyde intermediate, which was reacted with Me 3-dimethylamino-2-isocyanoacrylate, Me amine, and thioacetic acid; the resulting 1,3-thiazole-containing compound was deesterified and reacted with various amines or amino acids to give title product I.

AN 2004:41505 CAPLUS

DN 140:94300

TI Synthesis of tubulysin derivatives for therapeutic use in treatment of disease

IN Doemling, Alexander; Henkel, Bernd; Beck, Barbara; Illgen, Katrin; Sakamuri, Sukumar; Menon, Sanjay

PA Morphochem Aktiengesellschaft fur Kombinatorische Chemie, Germany

SO PCT Int. Appl., 65 pp.

CODEN: PIIXD2

DT Patent

LA German

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------|------|----------|-----------------|----------|
| PI WO 2004005327 | A1 | 20040115 | WO 2003-EP7419 | 20030709 |

W: AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KB, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TO, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

US 2002-366592P P 20020322

US 2003-US8888

2/3/05

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

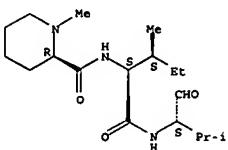
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 DE 2002-10230874 A 20020709
 DE 2002-10252719 A 20021113
 DE 10230874 A1 20040122 DE 2002-10230874 20020709
 DE 10252719 A1 20040527 DE 2002-10252719 20021113

OS MARPAT 140:94300

IT 644960-92-39
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of tubulosin derive. for therapeutic use in treatment of disease)

RN 644960-92-9 CAPLUS
 CN 2-Piperidinocarboxamide, N-[(1S,2S)-1-[(1S)-1-formyl-2-methylpropyl]amino]carbonyl]-2-methylbutyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG
 US 2002-3665922 P 20020322
 EP 2003-726101 20030321
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 US 2002-3665922 P 20020322
 WO 2003-US8888 W 20030321
 US 2003-667864 20030922
 US 2002-3665922 P 20020322
 WO 2003-US8888 A2 20030321

PATENT FAMILY INFORMATION:

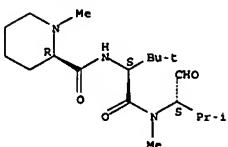
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| US 2004229819 | A1 | 20041118 | US (2003-667864 | 20030922 |
| | | | US 2002-3665922 | P 20020322 |
| | | | WO 2003-US8888 | A2 20030321 |
| WO 2003082268 | A2 | 20031009 | WO 2003-US8888 | 20030321 |
| WO 2003082268 | A3 | 20040923 | | |
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| US 2002-3665922 | P | 20020322 | | |

OS MARPAT 139:308008

IT 610786-68-0
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of hemiasterlin derive. as antitumor agents)

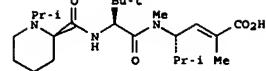
RN 610786-68-0 CAPLUS
 CN 2-Piperidinocarboxamide, N-[(1S)-1-[(1S)-1-formyl-2-methylpropyl]methylamino]carbonyl]-2,2-dimethylpropyl-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

GI



AB The invention provides compds. R1R2N(CR3R4)n-X1-NR5CHR6CONR7-R-X2-Q [R is an aliphatic, alicyclic, heteroaliph., heteroalicyclic, aryl or heteroaryl; n is 0-4; X1, X2 are CRARB, CO, or SO2, where RA, RB are H or R; R1, R2 are H, OH, CORC or R; RC is H, OH, ORD, or R; RD is R; R3, R4 are H or R; R5, R6, R7 are H, CORE or R; RB is H, OH, ORP, or R; RF is a group defined by R; R7 may be absent when R7 is linked to R via a double bond; two R1-R4 or two R5-R7 taken together may form a (hetero)alicyclic (hetero)alicyclic(heteroaryl), (hetero)alicyclic(heteroaryl), or (heteroaryl) moiety; Q is OQ', SRQ', NRQ'R'', N3, NOH, or R, where OQ' and RQ'' are or R or may combine as for R1-R4 or R5-R7 (with provisos) or their pharmaceutically acceptable derivs. for use in the treatment of cancer. Compds. of the invention, e.g., hemiasterlin derivative I, were prepared and assayed for inhibition of cell growth. Active compds. (IC50 < 20 nM) were evaluated in the reversibility, MDR, and mouse serum stability assays.

AN 2003-796473 CAPLUS
 DN 139:308008
 TI Preparation of hemiasterlin derivatives as antitumor agents
 IN Kowalczyk, James J.; Kuznetsov, Galina; Schiller, Shawn; Seletsky, Boris M.; Spyvee, Mark; Yang, Hu
 PA Eisai Co. Ltd., Japan
 SO PCT Int. Appl., 289 pp.

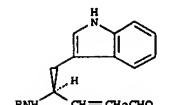
CODEN: PIXXD2
 DT Patent
 LA English

FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2003082268 | A2 | 20031009 | WO 2003-US8888 | 20030321 |
| WO 2003082268 | A3 | 20040923 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG | | | | |

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

GI



AB The present invention relates to scylamineraldehyde compds. of formula R4 -NH-CHR1-X-CHO [Q = one or two amino acid residual groups which may be substituted; R1 = hydrogen atom or an optionally substituted hydrocarbon or heterocyclic group; R4 = an optionally esterified carbonyl group or an acyl group; X = a optionally substituted straight-chain or branched divalent hydrocarbon group having a chain length of 1 to 4 atoms as the linear moiety, or salts thereof, which have strong cysteine protease inhibitory activities and are useful as prophylactic and therapeutic agent of various diseases, including bone diseases, caused by abnormal exasperation of cysteine protease, are prepared. Thus, 2.4 g N-tert-butoxycarbonyl-L-phenylalanyl-L-tryptophan and 1.76 g (formylmethoxy)triphenylphosphorane were dissolved in 10 mL THF and 30 mL toluene and stirred for 15 h to give the title compound (I; R = Boc-Phle). The latter compound and I (R = PhCH2O2C-Leu-Leu) (II) in vitro showed

IC50 of 3.5, 9.7 + 9.7 + 10-9 M, resp., against cathepsin L and that of 2.4 + 10-6 and 9.7 + 10-7 M, resp., against cathepsin B, resp. In a bone resorption inhibitory assay, they in vitro inhibited by 83 and 51%, resp., the Ca release from fetal rat's forearm bones. A gelatin capsule formulation containing II was described.

AN 1996:443908 CAPLUS

DN 125:115147

TI Preparation of peptide aldehyde derivatives as cysteine protease inhibitors
 IN Sodha, Takashi; Fujisawa, Yukio; Yasuma, Tsuneo; Mizoguchi, Junji
 PA Takeda Chemical Industries, Ltd., Japan
 SO PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| PI WO 9610014 | A1 | 19960404 | WO 1995-JP1933 | 19950925 |
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| RW: KE, MM, SD, SZ, UG, AT, BE, BG, CH, DE, DK, ES, PR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BP, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |

JP 1994-231639 A 19940927

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2/3/05

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

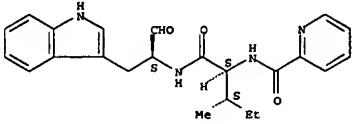
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| AU 9535341 | A1 19960419 | JP 1994-231839 | A 19940927 |
| | | AU 1995-35341 | 19950925 |
| | | JP 1994-231839 | A 19940927 |
| JP 08151355 | A2 19960611 | WO 1995-245957 | 19950925 |
| | | JP 1994-231839 | A 19940927 |
| EP 783489 | A1 19970716 | EP 1995-932288 | 19950925 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | JP 1994-231839 | A 19940927 |
| | | WO 1995-JP1933 | W 19950925 |

OS MARPAT 125:115147

IT 178911-01-8 CAPLUS
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide aldehyde derivs. as cysteine protease inhibitors and bone resorption inhibitors for treating bone diseases)

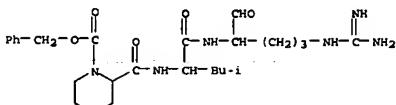
CN 2-Pyridinecarboxamide, N-[1-[(1-formyl-2-(1H-indol-3-yl)ethyl]amino]carbonyl]-, [1S-(R*,2R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 114332-79-5 CAPLUS
CN 1-Piperidinecarboxylic acid, 2-[[1-[[4-((aminoiminomethyl)amino)-1-formylbutyl]amino]carbonyl]-3-methylbutyl]amino]carbonyl-, phenylmethyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

AB Thirty analogs of leupeptin were synthesized and examined for their inhibitory activities against trypsin, papain, plasmin, kallikrein, thrombin, and urokinase *in vitro*. Relative to leupeptin, more benzoyl- and α -naphthalenesulfonyl-L-leucyl-L-argininal were 8-fold more inhibitory to papain, benzylxycarbonyl-L-pyroglutamyl-L-leucyl-L-argininal 10-fold more inhibitory to trypsin and plasmin, and DL-2-pipecolyl-L-leucyl-L-argininal 25-fold more inhibitory to kallikrein.

AB Against urokinase, only L-pyroglutamyl-L-leucyl-L-argininal exhibited a potent inhibitory activity. α -Naphthalenesulfonyl-, dansyl-, and benzylxycarbonyl-(2S,3R)-3-amino-2-hydroxy-4-phenylbutyryl-L-leucyl-L-argininal were inhibitory to thrombin.

AN 1988:200699 CAPLUS

DN 108:200699

TI Protease-inhibitory activities of leupeptin analogs

AU Saito, Tetsushi; Someno, Tetsuya; Ishii, Shinichi; Aoyagi, Takaaki; Umezawa, Hideo

CS Res. Lab., Nippon Kayaku Co., Ltd., Tokyo, 115, Japan

SO Journal of Antibiotics (1988), 41(2), 220-5

CODEN: JANTAJ; ISSN: 0021-8820

DT Journal

LA English

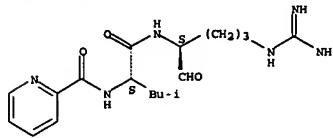
IT 83039-65-0 114318-20-6 114332-79-5

RL: BIOL (Biological study)
(protease inhibition by, other leupeptin analogs comparison with)

RN 83039-65-0 CAPLUS

CN 2-Pyridinecarboxamide, N-[1-[[4-((aminoiminomethyl)amino)-1-formylbutyl]amino]carbonyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

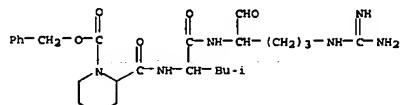
Absolute stereochemistry.



RN 114318-20-6 CAPLUS
CN 2-Piperidinocarboxamide, N-[1-[[4-((aminoiminomethyl)amino)-1-formylbutyl]amino]carbonyl]-3-methylbutyl] - (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 114332-79-5 CAPLUS
CN 1-Piperidinecarboxylic acid, 2-[[1-[[4-((aminoiminomethyl)amino)-1-formylbutyl]amino]carbonyl]-3-methylbutyl]amino]carbonyl-, phenylmethyl ester (9CI) (CA INDEX NAME)



AB L-Argininal peptides R-X-L-Leu-L-NHCH₂(CHO)(CH₂)₃NH₂ (I; X = CO₂; R = alkyl, cycloalkyl, (un)substituted Ph, (un)substituted naphthyl, pyridyl, PhCH₂O, furyl, thieryl, pyrrolidinyl, pyrrolidone moiety, diperidinyl [the latter 3 substituted with PhCH₂O₂C (2)], RIXI [X₁ = CH(OH), CH(NH₂); R₁ = alkyl, Ph, PhCH₂, ZNHCH₂(CH₂Ph)] were prepared as inhibitors of serine and thiol proteases. Thus, H-L-Leu-L-NHCH₂(CH₂OBu₂)(CH₂)₃NH₂HCl was condensed with Ba(OH)₂ di-Ph phosphorylazide in DMF at ambient temperature for 8 h and the resulting product

was hydrolyzed to give I-HCl (RX = Bz) (II). Data are given for the inhibition of papain, trypsin, kallikrein, and plasmin by I, e.g., II inhibited papain with an IC₅₀ of 0.5 mg/mL.

AN 1982:545287 CAPLUS

DN 97:145287

TI L-Argininal derivatives

IN Umezawa, H.; Takeuchi, T.; Aoyagi, T.; Ishii, S.; Seino, T.; Someno, T.

PA Nippon Kayaku Co., Ltd., Japan

SO Fr. Demande, 31 PP.

CODEN: PRXXBL

DT Patent

LA French

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|------------|
| PI PR 2490632 | A1 | 19820326 | FR 1981-17674 | 19810918 |
| PR 2490632 | B1 | 19861212 | | |
| JP 57054157 | A2 | 19820331 | JP 1980-129097 | A 19800919 |
| JP 02000342 | B4 | 19900108 | | 19800919 |
| US 4401594 | A | 19830830 | US 1981-300443 | 19810908 |
| | | | JP 1980-129097 | A 19800919 |
| GB 2086380 | A | 19820512 | GB 1981-28012 | 19810916 |
| GB 2086380 | B2 | 19840531 | | |
| DE 3137280 | A1 | 19820603 | JP 1980-129097 | A 19800919 |
| | | | DE 1981-3137280 | 19810918 |
| CA 1183130 | A1 | 19850226 | JP 1980-129097 | A 19800919 |
| | | | CA 1981-386220 | 19810918 |
| | | | JP 1980-129097 | A 19800919 |

OS CASREACT 97:145287

IT 83039-50-3P 83039-51-4P 83039-52-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and proteinase-inhibiting activity of)

RN 83039-50-3 CAPLUS

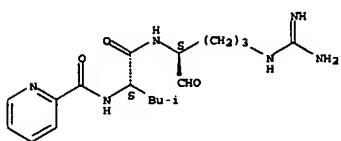
CN 2-Pyridinecarboxamide, N-[1-[[4-((aminoiminomethyl)amino)-1-formylbutyl]amino]carbonyl]-3-methylbutyl] - monohydrochloride, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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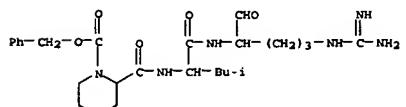
L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

(Continued)



● HCl

RN 83039-51-4 CAPLUS
CN 1-Piperidinocarboxylic acid, 2-{{1-[[4-[(aminoiminomethyl)amino]-1-formylbutyl]amino]carbonyl}-3-methylbutyl}amino}carbonyl-, phenylmethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

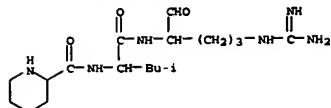


● HCl

RN 83039-52-5 CAPLUS
CN 2-Piperidinocarboxamide, N-{{1-[[4-[(aminoiminomethyl)amino]-1-formylbutyl]amino]carbonyl}-3-methylbutyl}, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

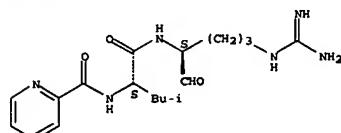
(Continued)



● HCl

IT 83039-65-0
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 83039-65-0 CAPLUS
CN 2-Pyridinecarboxamide, N-{{1-[[4-[(aminoiminomethyl)amino]-1-formylbutyl]amino]carbonyl}-3-methylbutyl}, {5-(R*,R*)}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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provided by InfoChem.

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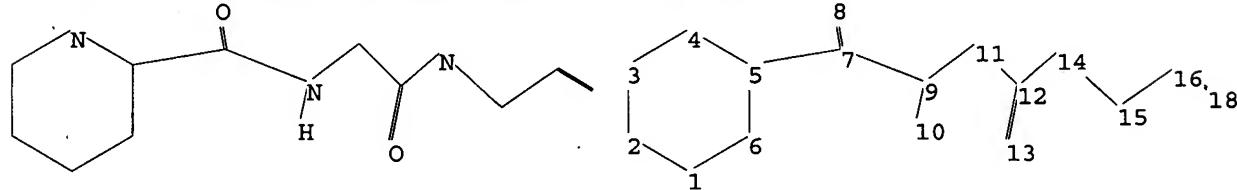
TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

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conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

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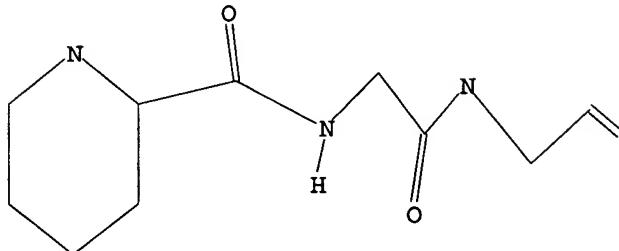
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L5 HAS NO ANSWERS

L5 STR



Structure attributes must be viewed using STN Express query preparation.

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41 ANSWERS

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FULL ESTIMATED COST

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FILE COVERS 1907 - 3 Feb 2005 VOL 142 ISS 6
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This file contains CAS Registry Numbers for easy and accurate substance identification.

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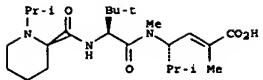
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L7 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
GI



AB The invention provides compds. R1R2N(CR3R4)n-X1-NR5CHR6CONR7-R-X2-Q [R is an aliphatic, alicyclic, heteroaliph., heterocyclic, aryl or heteroaryl moiety; n is 0-4; X1, X2 are CRARB, CO, or SO2, where RA, RB are H or R; R1, R2 are H, OH, CORC or R, where RC is H, OH, CORD, or R and RD is R; R3, R4 are H or R; R5, R6, R7 are H, CORE or R, where RE is H, OH, ORP, or R and RF is a group defined by R; R7 may be absent when NR7 is linked to R via a double bond; two R1-R4 or two RS-R7 taken together may form a (hetero)alicyclic, (hetero)alicyclic(aryl), or (hetero)aryl moiety; Q is ORQ', SRQ', NRQ'RO', N3, NOH, or R, where RO' and RO'' are H or R may combine as for R1-R4 or R5-R7 (with provisos!) or their pharmaceutically-acceptable derivs. for use in the treatment of cancer. Compds. of the invention, e.g., hemiesterlin derivative I, were prepared and assayed for inhibition of cell growth. Active compds. were evaluated in the reversibility, MDR, mouse serum stability, and other assays.

AN 2004:999664 CAPLUS

DN 141:395816

TI Preparation of hemiesterlin derivatives as antitumor agents
IN Kowalczyk, James K.; Kuznetsov, Galina; Schiller, Shawn; Seletsky, Boris M.; Spyvee, Mark; Yang, Hu

PA USA

SO U.S. Pat. Appl. Publ., 237 pp., Cont.-in-part of Appl. No.

PCT/US03/08888.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------|------|----------|-----------------|-------------|
| PI US 2004229819 | A1 | 20041118 | US 2003-667864 | 20030922 |
| | | | US 2003-366592P | P 20020322 |
| WO 2003082268 | A2 | 20031009 | WO 2003-US8888 | A2 20030321 |
| WO 2003082268 | A3 | 20040923 | WO 2003-US8888 | 20030321 |

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L7 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
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US 2003-366592P P 20020322

EP 1490054 A2 20041229 EP 2003-726101 20030321

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US 2002-366592P P 20020322

WO 2003-US8888 W 20030321

US 2004229819 A1 20041118 US 2003-667864 20030922

US 2002-366592P P 20020322

WO 2003-US8888 A2 20030321

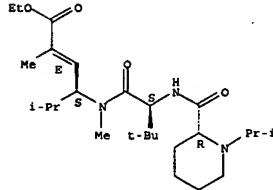
IT 610787-09-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of hemiesterlin derivs. as antitumor agents)

RN 610787-09-2 CAPLUS

CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[(1(R)-1-(1-methylethyl)-2-piperidinyl]carbonyl]amino]-1-oxobutyl)methylamino]-2,5-dimethyl-, (2E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L7 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



IT 610787-07-0P 610787-11-6P 610787-20-7P

610787-22-3P 610787-33-2P 610787-34-3P

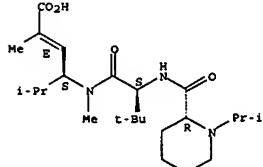
610787-35-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of hemiesterlin derivs. as antitumor agents)

RN 610787-07-0 CAPLUS

CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[(1(R)-1-(1-methylethyl)-2-piperidinyl]carbonyl]amino]-1-oxobutyl)methylamino]-2,5-dimethyl-, (2E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 610787-11-6 CAPLUS

CN 2-Hexenoic acid,

4-[(2S)-3,3-dimethyl-2-[(1(R)-1-(1-methylpropyl)-2-piperidinyl]carbonyl]amino]-1-oxobutyl)methylamino]-2,5-dimethyl-, (2E,4S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

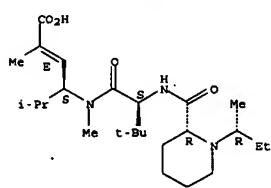
CRN 610787-10-5

CMF C25 H45 N3 O4

Absolute stereochemistry.

10667864

L7 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



CM 2

CRN 76-05-1

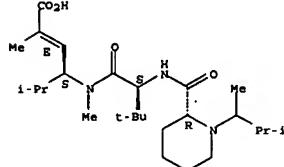
CMF C2 H F3 O2



RN 610787-20-7 CAPLUS

CN 2-Hexenoic acid, 4-[(2S)-2-[(1,2-dimethylpropyl)-2-piperidinyl]carbonyl]amino]-3,3-dimethyl-1-oxobutyl)methylamino]-2,5-dimethyl-, (2E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

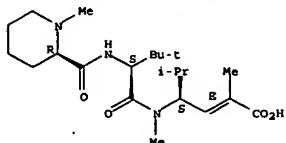


RN 610787-22-9 CAPLUS

CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[(1(R)-1-methyl-2-piperidinyl)carbonyl]amino]-1-oxobutyl)methylamino]-2,5-dimethyl-, (2E,4S)- (9CI) (CA INDEX NAME)

2/3/05

L7 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
Absolute stereochemistry.
Double bond geometry as shown.

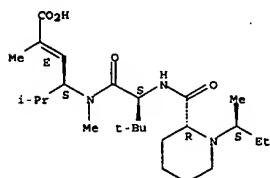


RN 610787-33-2 CAPLUS
CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[(1S)-1-methylpropyl]-2-piperidinyl]carbonyl|amino]-1-oxobutyl|methylamino]-2,5-dimethyl-, (2E,4S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 610787-32-1
CMP C25 H45 N3 O4

Absolute stereochemistry.
Double bond geometry as shown.



CM 2

CRN 76-05-1
CMP C2 H P3 O2

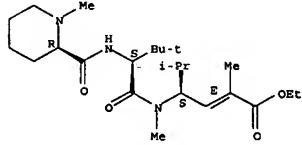
L7 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. or hemiaserin derive. as antitumor agents)

RN 610786-72-6 CAPLUS
CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[(1R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxobutyl|methylamino]-2,5-dimethyl-, ethyl ester, (2E,4S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 610786-71-5
CMP C24 H43 N3 O4

Absolute stereochemistry.
Double bond geometry as shown.



CM 2

CRN 76-05-1
CMP C2 H P3 O2

RN 610786-73-7 CAPLUS
CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[(1R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxobutyl|methylamino]-2,5-dimethyl-, monohydrochloride, (2E,4S)- (9CI) (CA INDEX NAME)

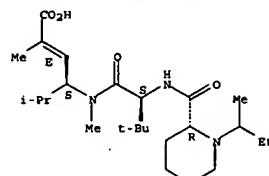
Absolute stereochemistry.
Double bond geometry as shown.

L7 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



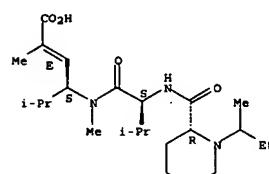
RN 610787-34-3 CAPLUS
CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[(1R)-1-(1-methylpropyl)-2-piperidinyl]carbonyl]amino]-1-oxobutyl|methylamino]-2,5-dimethyl-, (2E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 610787-35-4 CAPLUS
CN 2-Hexenoic acid, 2,5-dimethyl-4-[methyl|(2S)-3-methyl-2-[(1R)-1-(1-methylpropyl)-2-piperidinyl]carbonyl]amino]-, (2E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT 610786-72-6P 610786-73-7P 610786-82-8P

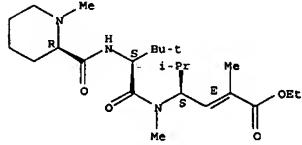
L7 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. or hemiaserin derive. as antitumor agents)

RN 610786-72-6 CAPLUS
CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[(1R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxobutyl|methylamino]-2,5-dimethyl-, ethyl ester, (2E,4S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 610786-71-5
CMP C24 H43 N3 O4

Absolute stereochemistry.
Double bond geometry as shown.



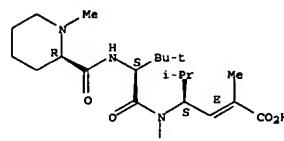
CM 2

CRN 76-05-1
CMP C2 H P3 O2

RN 610786-73-7 CAPLUS
CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[(1R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxobutyl|methylamino]-2,5-dimethyl-, monohydrochloride, (2E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

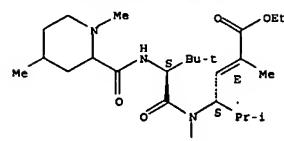
L7 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

RN 610786-82-8 CAPLUS
CN 2-Hexenoic acid, 4-[(2S)-2-[(1,4-dimethyl-2-piperidinyl)carbonyl]amino]-3,3-dimethyl-1-oxobutyl|methylamino]-2,5-dimethyl-, ethyl ester, (2E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 610787-17-2 CAPLUS
CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[(1R)-1-(1-methylpropyl)-2-piperidinyl]carbonyl]amino]-1-oxobutyl|methylamino]-2,5-dimethyl-, ethyl ester, (2E,4S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1
CRN 610787-16-1
CMP C27 H49 N3 O4

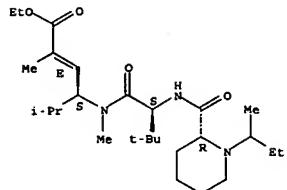
Absolute stereochemistry.
Double bond geometry as shown.

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L7 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

(Continued)



CM 2

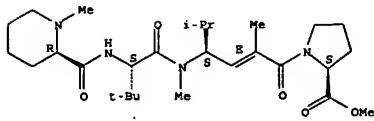
CRN 76-05-1
CMP C2 H F3 O2



IT 610786-74-BP 610786-95-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of hemisterlin derive. as antitumor agents)
RN 610786-74-8 CAPLUS
CN L-Proline,
(2R)-1-methyl-2-piperidinecarbonyl-3-methyl-L-valyl-(2E,4S)-2,5-dimethyl-4-(methylamino)-2-hexenoyl-, methyl ester, monohydrochloride
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

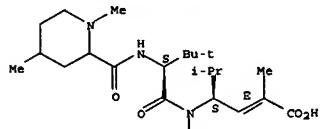
L7 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

RN 610786-95-3 CAPLUS
2-Hexenoic acid,
.4-[(2S)-2-[(1,4-dimethyl-2-piperidinyl)carbonyl]amino]-
3,3-dimethyl-1-oxobutyl)methylamino]-2,5-dimethyl-, (2E,4S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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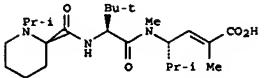
2/3/05

=> d abs fbib hitstr 2-9

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2/3/05

L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
GI



AB The invention provides compd. R1R2N(CR3R4)n-X1-NR5CHR6CONR7-R-X2-Q [R is an aliphatic, alicyclic, heteroaliph., heterocyclic, aryl or heteroaryl moiety; n is 0-4; X1, X2 are CRARB, CO, or SO2, where RA, RB are H or R; R1, R2 are H, OH, CORC or R; RC is H, OH, ORD, or R; RD is R; R3, R4 are H or R5; R6, R7 are H, CORE or R; RE is H, OH, ORP, or R; RP is a group defined by R; R7 may be absent when R7 is linked to R via a double bond; two R1-R4 or two R5-R7 taken together may form a (hetero)alicyclic, (hetero)alicyclic(aryl), (hetero)alicyclic(heteroaryl), or (hetero)aryl moiety; Q is ORQ', SRQ', NRQ'RO', NJ, NOH, or R, where RO' and RQ'' are H or R or may combine as for R1-R4 or R5-R7 (with provisos) or their pharmaceutically-acceptable derive. for use in the treatment of cancer. Compds. of the invention, e.g., hemiasterlin derivative I, were prepared and assayed for inhibition of cell growth. Active compd. (IC50 < 20 nM) were evaluated in the reversibility, MDR, and mouse serum stability assays.

AN 2003-7396473 CAPLUS
DN 139780808

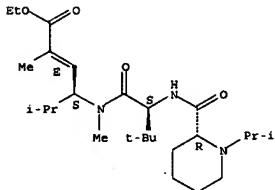
TI Preparation of hemiasterlin derivatives as antitumor agents
IN Kowalczyk, James J.; Kuznetsov, Galina; Schiller, Shawn; Seletsky, Boris M.; Spyvee, Mark; Yang, Hu
PA Eisai Co. Ltd., Japan
SO PCT Int. Appl., 289 pp.

CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 2

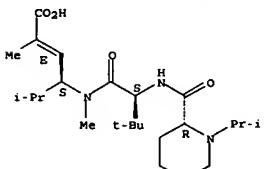
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------|------|----------|--|----------|
| PI WO 2003082268 | A2 | 20031009 | WO 2003-US8888 | 20030321 |
| WO 2003082268 | A3 | 20040923 | | |
| | | | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, LZ, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, | |

L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



IT 610787-07-0P 610787-11-6P 610787-20-7P
610787-22-9P 610787-33-3P 610787-34-3P
610787-35-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Uses)
(preparation of hemiasterlin derive. as antitumor agents)
RN 610787-07-0 CAPLUS
CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[([(2R)-1-(1-methylethyl)-2-piperidinyl]carbonyl]amino]-1-oxobutyl)methylamino]-2,5-dimethyl-, (2E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 610787-11-6 CAPLUS
CN 2-Hexenoic acid,
4-[(2S)-3,3-dimethyl-2-[([(2R)-1-[(1R)-1-methylpropyl]-2-piperidinyl]carbonyl]amino]-1-oxobutyl)methylamino]-2,5-dimethyl-, (2E,4S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 610787-10-5
CMF C25 H45 N3 O4

Absolute stereochemistry.

10667864

L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
BF, BJ, CP, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 2002-366592P P 20020322
EP 1490054 A2 20041229 EP 2003-726101 20030321
R: AT, BE, CH, DE, DK, ES, PR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, PI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
US 2002-366592P P 20020322
WO 2003-US8888 W 20030321
US 2003-667864 20030922
US 2002-366592P P 20020322
WO 2003-US8888 A2 20030321

PATENT FAMILY INFORMATION:

| FAN 2004-999664 | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------|------------|----------|---|----------------------------|------|
| PI US 2004229819 | A1 | 20041118 | US 2003-667864 20030922 | US 2002-366592P P 20020322 | |
| | | | WO 2003-US8888 A2 20030321 | | |
| HO 2003082268 | A2 | 20031009 | WO 2003-US8888 20030321 | | |
| HO 2003082268 | A3 | 20040923 | | | |
| | | | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, LZ, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | |
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OS MARPAT 139-308008

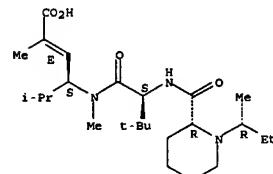
IT 610787-09-28
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of hemiasterlin derive. as antitumor agents)

RN 610787-09-2 CAPLUS

CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[([(2R)-1-(1-methylethyl)-2-piperidinyl]carbonyl]amino]-1-oxobutyl)methylamino]-2,5-dimethyl-, ethyl ester, (2E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
Double bond geometry as shown.



CM 2

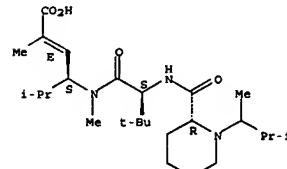
CRN 76-05-1
CMF C2 H3 F O2



RN 610787-20-7 CAPLUS

CN 2-Hexenoic acid, 4-[(2S)-2-[([(2R)-1-(1,2-dimethylpropyl)-2-piperidinyl]carbonyl]amino]-3,3-dimethyl-1-oxobutyl)methylamino]-2,5-dimethyl-, (2E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

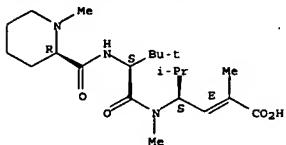


RN 610787-22-9 CAPLUS

CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[([(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxobutyl)methylamino]-2,5-dimethyl-, (2E,4S)- (9CI) (CA INDEX NAME)

2/3/05

L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
Absolute stereochemistry.
Double bond geometry as shown.

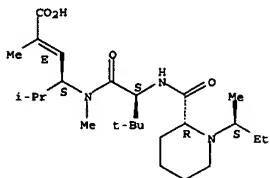


RN 610787-33-2 CAPLUS
CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[(1S)-1-methylpropyl]-2-piperidinyl]carbonyl-amino-1-oxobutyl-methylamino-2,5-dimethyl-, (2E,4S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 610787-32-1
CMF C25 H45 N3 O4

Absolute stereochemistry.
Double bond geometry as shown.



CM 2

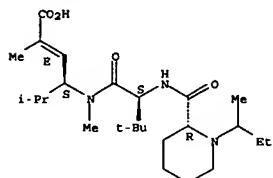
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CMF C2 H F3 O2

L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



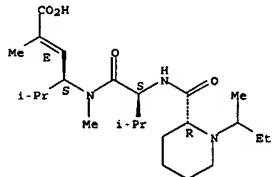
RN 610787-34-3 CAPLUS
CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[(1S)-1-(1-methylpropyl)-2-piperidinyl]carbonyl]amino-1-oxobutyl-methylamino-2,5-dimethyl-, (2E,4S)-, (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 610787-35-4 CAPLUS
CN 2-Hexenoic acid, 2,5-dimethyl-4-(methyl)(2S)-3-methyl-2-[(1S)-1-(1-methylpropyl)-2-piperidinyl]carbonyl]amino-1-oxobutyl-, (2E,4S)-, (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT 610786-72-6P 610786-73-7P 610786-82-8P

L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
610787-17-2P

RL: RCT (Reactant); SPA (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of hemisterlin derivs. as antitumor agents)

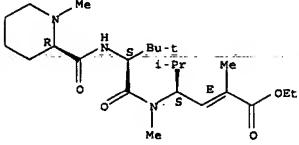
RN 610786-72-6 CAPLUS

CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[(1S)-1-methyl-2-piperidinyl]carbonyl]amino-1-oxobutyl-methylamino-2,5-dimethyl-, ethyl ester, (2E,4S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 610786-71-5
CMF C24 H43 N3 O4

Absolute stereochemistry.
Double bond geometry as shown.



CM 2

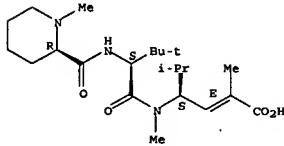
CRN 76-05-1
CMF C2 H F3 O2



RN 610786-73-7 CAPLUS
CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[(1S)-1-methyl-2-piperidinyl]carbonyl]amino-1-oxobutyl-methylamino-2,5-dimethyl-, monohydrochloride, (2E,4S)-, (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

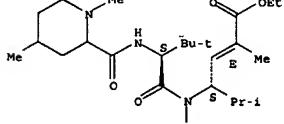
L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

RN 610786-82-8 CAPLUS
CN 2-Hexenoic acid, 4-[(1,4-dimethyl-2-piperidinyl)carbonyl]amino-3,3-dimethyl-1-oxobutyl-methylamino-2,5-dimethyl-, ethyl ester, (2E,4S)-, (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 610786-17-2 CAPLUS
CN 2-Hexenoic acid, 4-[(2S)-3,3-dimethyl-2-[(1S)-1-(1-methylpropyl)-2-piperidinyl]carbonyl]amino-1-oxobutyl-methylamino-2,5-dimethyl-, ethyl ester, (2E,4S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

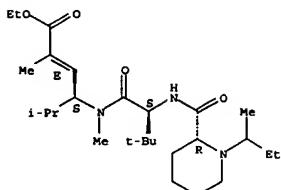
CRN 610787-16-1
CMF C27 H49 N3 O4

Absolute stereochemistry.
Double bond geometry as shown.

10667864

2/3/05

L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



CM 2

CRN 76-05-1
CMF C2 H P3 O2

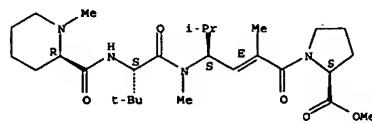


IT 610786-74-8P 610786-55-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of hemisterlin derivs. as antitumor agents)
RN 610786-74-8 CAPLUS
CN L-Proline,
(2R)-1-methyl-2-piperidinecarbonyl-3-methyl-L-valyl-(2E,4S)-2,5-dimethyl-4-(methylamino)-2-hexenoyl-, methyl ester, monohydrochloride
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

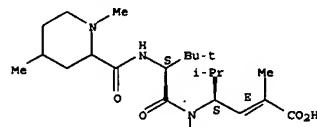


● HCl

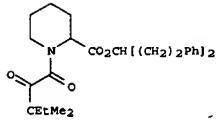
RN 610786-95-3 CAPLUS

CN 2-Hexenoic acid,
4-[(1S)-2-[(1,4-dimethyl-2-piperidinyl)carbonyl]amino]-
3,3-dimethyl-1-oxobutyl)methylamino]-2,5-dimethyl-, (2E,4S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L7 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
GI



AB Pipecolic acid derivs. are prepared for treating vision disorders, improving vision, treating memory impairment, or enhancing memory performance in an animal. These compds. bind to immunophilin FKBP12 and preferably do not have immunosuppressive activity. Affinity for FKBP12 is measured as inhibition of prolyl peptidyl-cis-trans-isomerase (rotamase). Thus, pipecolic acid ester I inhibited rotamase with a Ki of 20 nM, showed a clearance rate of 41.8 μL/min, and rescued 56.6% of optic nerve axons from degeneration 14 days after optic nerve transection in rats (dose and route of administration not stated).

AN 2000:133482 CAPLUS

DN 132:175851

TI Pipecolic acid derivatives for vision and memory disorders
IN Ross, Douglas T.; Sauer, Hansjorg; Hamilton, Gregory S.; Steiner, Joseph P.

PA Guilford Pharmaceuticals Inc., USA
SO PCT Int. Appl., 126 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| PI WO 2000009109 | A2 | 20000224 | WO 1999-US18242 | 19990812 |
| WO 2000009109 | A3 | 20000817 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DN, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
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| US 6376517 | B1 | 20020423 | US 1998-134417 | A 19980814 |
| CA 2344520 | AA | 20000224 | CA 1999-2344520 | 19990812 |
| | | | US 1998-134417 | A 19980814 |
| | | | WO 1999-US18242 | W 19990812 |
| AU 9955557 | A1 | 20000306 | AU 1999-55557 | 19990812 |
| | | | US 1998-134417 | A 19980814 |
| | | | WO 1999-US18242 | W 19990812 |
| EP 1109554 | A2 | 20010627 | EP 1999-942109 | 19990812 |

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L7 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, PI, RO

US 1998-134417 A 19980814
WO 1999-US18242 W 19990812
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WO 1999-US18242 W 19990812

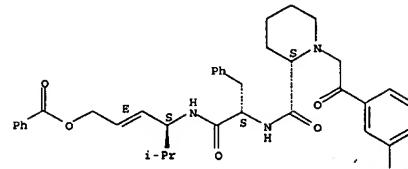
IT 145021-65-4 145021-66-5 145021-67-6

145021-68-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(pipecolic acid derive. for vision and memory disorders)

145021-65-4
CN 2-Piperidinecarboxamide, N-[(1S)-2-[(1S,2E)-4-(benzyloxy)-1-(1-methylethyl)-2-buteneyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-1-[2-(3-methoxyphenyl)-2-oxoethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 145021-66-5 CAPLUS

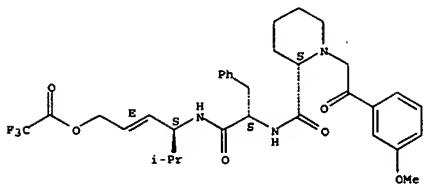
CN Acetic acid, trifluoro-,
(2E,4S)-4-[(1S)-2-[(1S,2E)-4-(benzyloxy)-1-(1-methylethyl)-2-buteneyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-1-oxo-3-phenylpropylamino]-5-methyl-2-hexenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

2/3/05

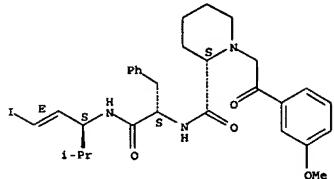
L7 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

(Continued)



RN 145021-67-6 CAPLUS
 CN 2-Piperidinecarboxamide, N-[(1S)-2-[(1S,2E)-3-iodo-1-(1-methylethyl)-2-propenyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-1-[2-(3-methoxyphenyl)-2-oxoethyl]-, (2S)- (9CI) (CA INDEX NAME)

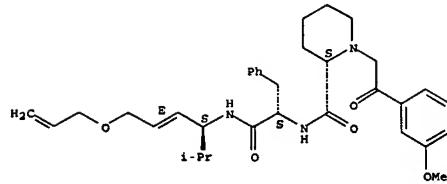
Absolute stereochemistry.
 Double bond geometry as shown.



RN 145021-68-7 CAPLUS
 CN 2-Piperidinecarboxamide, 1-[2-(3-methoxyphenyl)-2-oxoethyl]-N-[(1S)-2-[(1S,2E)-1-(1-methylethyl)-4-(2-propenoxy)-2-butene]amino]-2-oxo-1-(phenylmethyl)ethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

L7 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

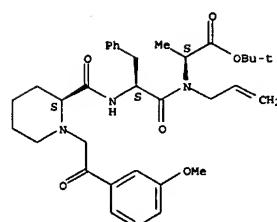


L7 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
 AB This invention relates to pharmaceutical compns. and methods for treating alopecia and promoting hair growth using piperolic acid derivs. Thus, a hair lotion contained 95% EtOH, a piperolic acid derivative such as 4-(4-methoxyphenyl)butyl 1-(2-oxo-2-phenylacetyl)-2-piperidinecarboxylate 10.0, α -tocopherol acetate 0.01, ethoxylated hardened castor oil 0.5, and water 9.0, and perfume and dye.
 AN 1999-783903 CAPLUS
 DN 132-26633
 TI Piperolic acid derivatives for hair growth compositions
 IN Hamilton, Gregory S.; Steiner, Joseph P.
 PA Guilford Pharmaceuticals, Inc., USA
 SO PCT Int. Appl., 103 PP.
 CODEN: PIXXD2
 Patent
 LA English
 FAN. CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| PI WO 9962483 | A1 | 19991209 | WO 1998-US11242 | 19980603 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MM, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2333698 | AA | 19991209 | CA 1998-2333698 | 19980603 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MM, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9877167 | A1 | 19991220 | AU 1998-77167 | 19980603 |
| AU 761083 | B2 | 20030529 | | |
| EP 1083872 | A1 | 20010321 | WO 1998-US11242 | A 19980603 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | EP 1998-925152 | 19980603 |
| JP 2002516839 | T2 | 20020611 | WO 1998-US11242 | W 19980603 |
| | | | JP 2000-551739 | 19980603 |
| | | | WO 1998-US11242 | W 19980603 |
| IT 252002-98-5 252002-99-6 252003-00-2
252003-01-3 252003-02-4
RL: BUN (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(piperolic acid derivs. for hair growth compns.) | | | | |
| RN 252002-98-5 CAPLUS
CN L-Alanine,
(2S)-1-(2-(3-methoxyphenyl)-2-oxoethyl)-2-piperidinecarbonyl-L-phenylalanyl-N-2-propenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME) | | | | |

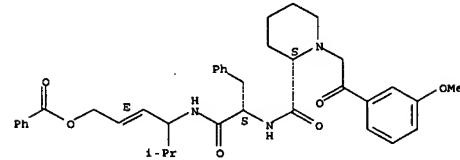
Absolute stereochemistry.

L7 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 252002-99-6 CAPLUS
 CN 2-Piperidinecarboxamide, N-[(1S)-2-[(2E)-4-(benzoyloxy)-1-(1-methylethyl)-2-butenyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-1-[2-(3-methoxyphenyl)-2-oxoethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



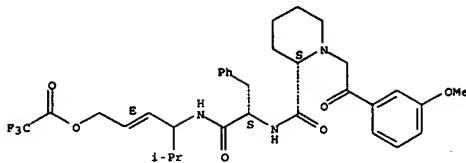
RN 252003-00-2 CAPLUS
 CN Acetic acid, trifluoro-,
 (2E)-4-[[2S]-2-[[[2S]-1-(2-(3-methoxyphenyl)-2-oxoethyl)-2-piperidinyl]carbonylamino]-1-oxo-3-phenylpropyl]amino]-5-methyl-2-hexenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

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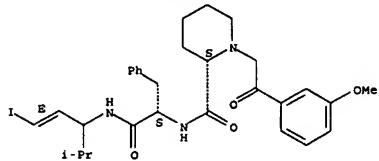
2/3/05

L7 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



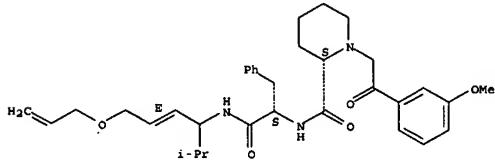
RN 252003-01-3 CAPLUS
 CN 2-Piperidinecarboxamide, N-[(1S)-2-[(2E)-3-iodo-1-(1-methylethyl)-2-propenyl]amino]-2-oxo-1-(phenylmethyl)ethyl-1-[2-(3-methoxyphenyl)-2-oxoethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



RN 252003-02-4 CAPLUS
 CN 2-Piperidinecarboxamide, 1-(2-(3-methoxyphenyl)-2-oxoethyl)-N-[(1S)-2-[(2E)-1-(1-methylethyl)-4-(2-propenyl)oxy]-2-buteneyl]amino]-2-oxo-1-(phenylmethyl)ethyl-, (2S) (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



L7 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
 AB Rotamase or peptidyl-prolyl isomerase inhibitors e.g. neurotrophic
 pipecolinic acid derivs. (including PK506, May 124666, Rapamycin, SLB
 506,
 etc.) with FKBP-type immunophilin affinity are claimed for stimulating
 nerve growth and regeneration after nerve injury in treatment of neurod.
 diseases e.g. Alzheimer's disease, parkinsonism, muscle atrophy, etc.
 The effects of these inhibitors were comparable to that of nerve growth
 factor.

AN 1997:165074 CAPLUS
 DN 126:152815
 TI Rotamase inhibitors for treatment of neurological diseases
 IN Steiner, Joseph P.; Synder, Solomon; Hamilton, Gregory S.
 PA Guilford Pharmaceuticals, Inc., USA; Johns Hopkins University School of
 Medicine
 SO Jpn. Kokai Tokkyo Koho, 41 pp.
 CODEN: JKXXJP
 DT Patent
 LA Japanese
 PAN.CNT 3

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|------------|
| JP 08333256 | A2 | 19961217 | JP 1996-132866 | 19960430 |
| JP 3060373 | B2 | 20000710 | | |
| US 5798355 | A | 19980825 | US 1995-474072 | A 19950607 |
| CN 1187127 | A | 19980708 | US 1996-194555 | 19960605 |
| LT 4516 | B | 19990625 | US 1995-474072 | A 19950607 |
| | | | LT 1998-2 | 19980106 |
| | | | US 1995-474072 | A 19950607 |

PATENT FAMILY INFORMATION:
 PAN 1997:151523
 PATENT NO. KIND DATE APPLICATION NO. DATE

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 9640140 | A1 | 19961219 | WO 1996-US9561 | 19960605 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG | | | | |
| RW: KE, LS, MM, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CW, CO, CI, CM, GA, GN | | | | |
| US 5798355 | A | 19980825 | US 1995-474072 | A 19950607 |
| US 5696135 | A | 19971209 | US 1996-653905 | 19960528 |
| AU 9661622 | A1 | 19961230 | US 1995-474072 | A 19950607 |
| AU 710423 | B2 | 19990923 | AU 1996-61622 | 19960605 |
| GB 2305605 | A1 | 19970416 | US 1995-474072 | A 19950607 |
| GB 2305605 | B2 | 20000112 | GB 1996-24258 | 19960605 |
| DE 19680255 | T | 19970605 | US 1995-474072 | A 19950607 |
| | | | US 1996-653905 | A 19960528 |
| | | | US 1995-474072 | A 19950607 |
| | | | US 1996-653905 | A 19960528 |
| | | | US 1996-653905 | A 19960528 |
| | | | US 1996-653905 | A 19960528 |

L7 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
 WO 1996-US9561 W 19960605
 EP 777478 A1 19970611 EP 1996-919227 19960605
 EP 777478 B1 20011107 R: BE, PR, GR, IE, IT, MC, NL

| EP 777478 | A1 | 19970611 | EP 1996-919227 | 19960605 |
|-----------|----|----------|---|------------|
| | | | US 1995-474072 | A 19950607 |
| | | | US 1996-653905 | A 19960528 |
| | | | WO 1996-US9561 | W 19960605 |
| | | | BR 1996-8485 | 19960605 |
| | | | US 1995-474072 | A 19950607 |
| | | | US 1996-653905 | A 19960528 |
| | | | WO 1996-US9561 | W 19960605 |
| | | | FI 1996-4137 | 19961015 |
| | | | US 1995-474072 | A 19950607 |
| | | | US 1996-653905 | A 19960528 |
| | | | WO 1996-US9561 | W 19960605 |
| | | | NZ 310767 A 20001124 | 19960605 |
| | | | US 1995-474072 | A 19950607 |
| | | | US 1996-653905 | A 19960528 |
| | | | WO 1996-US9561 | W 19960605 |
| | | | FI 9604137 A 19970115 | 19961018 |
| | | | US 1995-474072 | A 19950607 |
| | | | US 1996-653905 | A 19960528 |
| | | | WO 1996-US9561 | W 19960605 |
| | | | TW 523410 B 20030311 | 1996024 |
| | | | US 1995-474072 | A 19950607 |
| | | | US 1996-653905 | A 19960528 |
| | | | WO 1996-US9561 | W 19960605 |
| | | | SE 9604097 A 19961208 | 19960605 |
| | | | US 1995-474072 | A 19950607 |
| | | | US 1996-653905 | A 19960528 |
| | | | WO 1996-US9561 | W 19960605 |
| | | | DK 9601256 A 19961220 | 19961108 |
| | | | US 1995-474072 | A 19950607 |
| | | | US 1996-653905 | A 19960528 |
| | | | WO 1996-US9561 | W 19960605 |
| | | | NO 9704290 A 19971204 | 19970917 |
| | | | US 1995-474072 | A 19950607 |
| | | | US 1996-653905 | A 19960528 |
| | | | WO 1996-US9561 | W 19960605 |
| | | | HK 1013254 A1 20000616 | 19981222 |
| | | | US 1995-474072 | A 19950607 |
| | | | US 1996-653905 | A 19960528 |
| | | | WO 1996-US9561 | W 19960605 |
| | | | PAN 1998:17977 | |
| | | | PATENT NO. KIND DATE APPLICATION NO. DATE | |
| | | | PI 5696135 A 19971209 US 1996-653905 19960528 | |
| | | | PI 5798355 A 19980825 US 1995-474072 A2 19950607 | |
| | | | CA 2206824 AA 19961219 CA 1996-2206824 19960605 | |
| | | | CA 2206824 C 20010814 US 1995-474072 A 19950607 | |
| | | | WO 9640140 A1 19961219 WO 1996-US9561 19960605 | |
| | | | W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG | |
| | | | RW: KE, LS, MM, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CW, CO, CI, CM, GA, GN | |
| | | | US 1995-474072 A 19950607 | |
| | | | US 1996-653905 A 19960528 | |
| | | | AU 9661622 A1 19961230 AU 1996-61622 19960605 | |

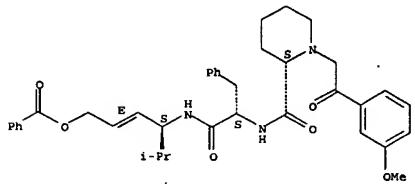
10667864

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| L7 | ANSWER 5 OF 9 | CAPLUS | COPYRIGHT 2005 ACS on STN | (Continued) |
|-------------------------------|---------------|----------|--|---|
| AU 710423 | B2 | 19990923 | US 1995-474072 A 19950607
US 1996-653905 A 19960528
WO 1996-US9561 W 19960605
GB 2305605 A1 19970416 GB 1996-24258 19960605 | |
| GB 2305605 | B2 | 20000112 | US 1995-474072 A 19950607
US 1996-653905 A 19960528
WO 1996-US9561 W 19960605 | |
| DE 19680255 | T | 19970605 | DE 1996-19680255 19960605
US 1995-474072 A 19950607
US 1996-653905 A 19960528
WO 1996-US9561 W 19960605 | |
| EP 777478 | A1 | 19970611 | EP 1996-919227 19960605 | LT 4516 B 19990625 LT 1998-2
EP 777478 B1 20011107 |
| R: BE, PR, GR, IE, IT, MC, NL | | | | LV 11986 B 19980920 LV 1997-244 |
| CN 1187127 | A | 19980708 | US 1995-474072 A 19950607
US 1996-653905 A 19960528
WO 1996-US9561 W 19960605 | ES 2194596 A1 20031116 ES 2001-200150041
CN 1996-194555 19960605
US 1995-474072 A 19950607 |
| CH 689541 | A | 19990615 | CH 1996-2789 19960605
US 1995-474072 A 19950607
US 1996-653905 A 19960528 | US 6022878 A 20000208 US 1998-113330
US 1995-474072 A 19950607
US 1996-653905 A 19960528 |
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WO 1996-US9561 W 19960605 | HK 1013254 A1 20000616 HK 1998-114579
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WO 1996-US9561 W 19960605 |
| ES 2138518 | A1 | 20000101 | ES 1996-50031 19960605 | AU 9948793 A1 19991125 AU 1999-48793 19990916 |
| ES 2138518 | B1 | 20010101 | US 1995-474072 A 19950607
US 1996-653905 A 19960528 | AU 740089 B2 20011101 US 1995-474072 A 19950607
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| NZ 310767 | A | 20001124 | NZ 1996-310767 19960605
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US 1996-653905 A 19960528
WO 1996-US9561 W 19960605 | US 2002052372 A1 20020502 US 1999-435323
AU 1996-61622 A3 19960605
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US 1996-653905 A 19960528
WO 1996-US9561 W 19960605 |
| ES 2166740 | A1 | 20020416 | ES 2000-200050035 19960605 | US 2003114365 A1 20030619 US 2002-228312 20020827
US 1995-474072 A 19950607
US 1996-653905 A 19960528 |
| ES 2166740 | B1 | 20031101 | PI 1996-4137 19961015
US 1995-474072 A 19950607
US 1996-653905 A 19960528
WO 1996-US9561 W 19960605 | IT 145021-65-4 145021-66-5 145021-67-6
145021-68-7
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);
USES
(Uses)
(rotamase inhibitors for treatment of neurol. diseases)
RN 145021-65-4 CAPLUS
CN 2-Piperidinecarboxamide, N-[(1S)-2-((1S,2E)-4-(benzoyloxy)-1-(1- |
| FI 9604137 | A | 19970115 | PI 1996-4137 19961015
US 1995-474072 A 19950607
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WO 1996-US9561 W 19960605 | US 2003114365 A1 20030619 US 2002-228312 20020827
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US 1996-653905 A 19960528
US 1997-787162 A1 19970123
US 1998-113330 A1 19980710
US 1999-435323 A3 19991105 |
| TW 523410 | B | 20030311 | TW 1996-85113075 19961024
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US 1996-653905 A 19960528
WO 1996-US9561 W 19960605 | |
| ZA 9608981 | A | 19980525 | ZA 1996-8981 19961025
US 1996-653905 A 19960528 | |
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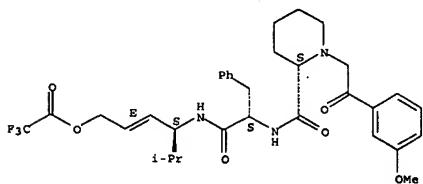
L7 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
methylmethoxyphenyl)-2-oxoethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 145021-66-5 CAPLUS
CN Acetic acid, trifluoro-, (2E,4S)-4-[(2S)-2-[(2S)-1-[2-(3-methoxyphenyl)-2-oxoethyl]-2-piperidinylcarbonyl]amino]-1-oxo-3-phenylpropyl]amino]-5-methyl-2-hexenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

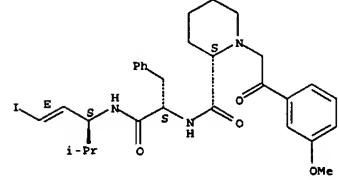


RN 145021-67-6 CAPLUS
CN 2-Piperidinecarboxamide, N-[(1S)-2-[(1S,2E)-3-iodo-1-(1-methylethyl)-2-propenyl]amino]-2-oxo-1-(phenylmethyl)ethyl)-1-[2-(3-methoxyphenyl)-2-oxoethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

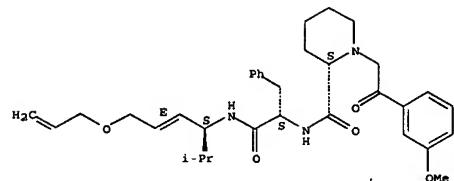
| L7 | ANSWER 5 OF 9 | CAPLUS | COPYRIGHT 2005 ACS on STN | (Continued) |
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US 1996-653905 A 19960528
WO 1996-US9561 W 19960605
US 5843960 A 19981201 US 1997-787162 A2 19950607
US 1995-474072 A 19950607
US 1996-653905 A 19960528
WO 1996-US9561 W 19960605 | |
| GB 2305605 | B2 | 20000112 | US 1995-474072 A 19950607
US 1996-653905 A 19960528
WO 1996-US9561 W 19960605 | |
| DE 19680255 | T | 19970605 | DE 1996-19680255 19960605
US 1995-474072 A 19950607
US 1996-653905 A 19960528
WO 1996-US9561 W 19960605 | |
| EP 777478 | A1 | 19970611 | EP 1996-919227 19960605 | LT 4516 B 19990625 LT 1998-2
EP 777478 B1 20011107 |
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| CN 1187127 | A | 19980708 | US 1995-474072 A 19950607
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WO 1996-US9561 W 19960605 | ES 2194596 A1 20031116 ES 2001-200150041
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US 1995-474072 A 19950607 |
| CH 689541 | A | 19990615 | CH 1996-2789 19960605
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US 1996-653905 A 19960528
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US 1995-474072 A 19950607
US 1996-653905 A 19960528 |
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US 1995-474072 A 19950607
US 1996-653905 A 19960528
WO 1996-US9561 W 19960605 | IT 145021-65-4 145021-66-5 145021-67-6
145021-68-7
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);
USES
(Uses)
(rotamase inhibitors for treatment of neurol. diseases)
RN 145021-65-4 CAPLUS
CN 2-Piperidinecarboxamide, N-[(1S)-2-((1S,2E)-4-(benzoyloxy)-1-(1- |
| FI 9604137 | A | 19970115 | PI 1996-4137 19961015
US 1995-474072 A 19950607
US 1996-653905 A 19960528
WO 1996-US9561 W 19960605 | US 2003114365 A1 20030619 US 2002-228312 20020827
US 1995-474072 A 19950607
US 1996-653905 A 19960528
US 1997-787162 A1 19970123
US 1998-113330 A1 19980710
US 1999-435323 A3 19991105 |
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US 1995-474072 A 19950607
US 1996-653905 A 19960528
WO 1996-US9561 W 19960605 | |
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US 1996-653905 A 19960528 | |
| SE 9604097 | A | 19961208 | SE 1996-4097 19961108
US 1995-474072 A 19950607
US 1996-653905 A 19960528
WO 1996-US9561 W 19960605 | |
| DK 9601256 | A | 19961220 | DK 1996-1256 19961108 | |

L7 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 145021-68-7 CAPLUS
CN 2-Piperidinecarboxamide, 1-[2-(3-methoxyphenyl)-2-oxoethyl]-N-[(1S)-2-((1S,2E)-1-(1-methylethyl)-4-(2-propenyl)oxy)-2-buteneyl]amino]-2-oxo-1-(phenylmethyl)ethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



2/3/05

L7 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
 AB Neurotrophic pipelicolic acid deriva. having an affinity for FKBP-type immunophilins are useful as inhibitors of the enzyme activity associated with immunophilin proteins, and in particular inhibitors of peptidyl-prolyl isomerase or rotamase enzyme activity, to stimulate or promote neuronal growth or regeneration. The compds. of the invention (e.g. Way-124,666; SLB-506) are useful for the treatment of neurol. disorders. The compds. may be used in conjunction with a neurotrophic factor (neurotrophic growth factor, brain-derived growth factor, neurotrophin-3, etc.).

AN 1997-151523 CAPLUS

DN 126:152817

TI Pipelicolic acid derivatives as inhibitors of rotamase activity, and use in treatment of nervous system disorders.

IN Steiner, Joseph P.; Snyder, Solomon; Hamilton, Gregory S.

PA Guilford Pharmaceuticals Inc., USA; Johns Hopkins University School of Medicine

SO PCT Int. Appl., 110 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|------------|
| PI WO 9640140 | A1 | 19961219 | WO 1996-US9561 | 19960605 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MM, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG | | | | |
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| US 5798355 | A | 19980825 | US 1995-474072 | 19950607 |
| US 5696135 | A | 19971209 | US 1996-653905 | 19960528 |
| AU 9661622 | A1 | 19961230 | AU 1996-61622 | 19960605 |
| AU 710423 | B2 | 19990923 | US 1995-474072 | A 19950607 |
| | | | US 1996-653905 | A 19960528 |
| GB 2305605 | A1 | 19970416 | GB 1996-24258 | 19960605 |
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L7 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
 WO 9640140 A1 19961219 WO 1996-US9561 19960605
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L7 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

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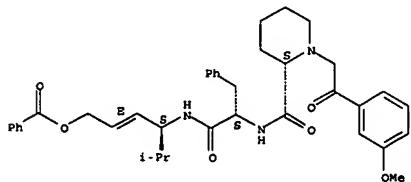
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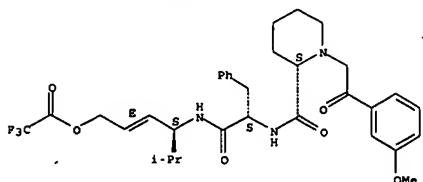
L7 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
treatment of nervous system disorders.)
RN 145021-65-4 CAPLUS
CN 2-Piperidinocarboxamide, N-[(1S)-2-[(1S,2R)-4-(benzoyloxy)-1-(1-methylethyl)-2-butyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-1-(2-(3-methoxyphenyl)-2-oxoethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 145021-66-5 CAPLUS
CN Acetic acid, trifluoro-, (2E,4S)-4-[(2S)-2-[(2-(3-methoxyphenyl)-2-oxoethyl)-2-piperidinyl]carbonyl]amino]-1-oxo-3-phenylpropylamino]-5-methyl-2-hexenyl ester (9CI) (CA INDEX NAME)

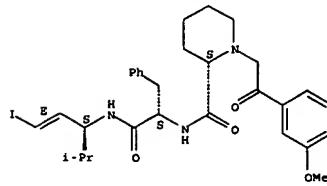
Absolute stereochemistry.
Double bond geometry as shown.



RN 145021-67-6 CAPLUS
CN 2-Piperidinocarboxamide, N-[(1S)-2-[(1S,2E)-3-iodo-1-(1-methylethyl)-2-propenyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-1-(2-(3-methoxyphenyl)-2-oxoethyl)-, (2S)- (9CI) (CA INDEX NAME)

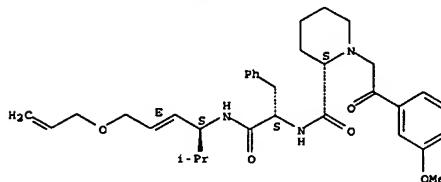
Absolute stereochemistry.
Double bond geometry as shown.

L7 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

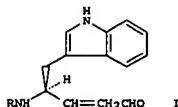


RN 145021-68-7 CAPLUS
CN 2-Piperidinocarboxamide, 1-[2-(3-methoxyphenyl)-2-oxoethyl]-N-[(1S)-2-[(1S,2E)-1-(1-methylethyl)-4-(2-propenyl)oxy]-2-butyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L7 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
GI



AB The present invention relates to acylaminoaldehyde compds. of formula R4-Q-NHCHR1-X-CHO IQ = one or two amino acid residual groups which may be substituted; R1 = hydrogen atom or an optionally substituted hydrocarbon or heterocyclic group; R4 = an optionally esterified carboxyl group or an acyl group; X = a optionally substituted straight-chain or branched divalent hydrocarbon group having a chain length of 1 to 4 atoms as the linear moiety), or salts thereof, which have strong cysteine protease inhibitory activities and are useful as prophylactic and therapeutic agent of various diseases, including bone diseases, caused by abnormal exasperation of cysteine protease, are prepared. Thus, 2.4 g N-tert-butoxycarbonyl-L-phenylalanyl-L-tryptophan and 1.76 g (formylmethylene)triphenylphosphonium were dissolved in 10 mL THF and 30 mL toluene and stirred for 15 h to give the title compound (I; R = Boc-Phe).

The latter compound and I (R = PhCH2O2C-Leu-Leu) (II) in vitro showed IC50 of 3.5 + 10-8 and 9.7 + 10-9 M, resp., against cathepsin L and that of 2.4 + 10-6 and 9.7 + 10-7 M, resp., against cathepsin B, resp. In a bone resorption inhibitory assay, they in vitro inhibited by 83 and 51%, resp., the Ca release from fetal rat's forearm bones. A gelatin capsule formulation containing II was described.

AN 19961443908 CAPLUS

DN 125:115147

TI Preparation of peptide aldehyde derivatives as cysteine protease inhibitors

IN Sohda, Takashi; Fujisawa, Yukio; Yasuma, Tsuneo; Mizoguchi, Junji

PA Takeda Chemical Industries, Ltd., Japan

SO PCT Int. Appl., 85 pp.

CODEN: PIXKD2

DT Patent

LA English

PATENT CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| PI WO 9610014 | A1 | 19960404 | WO 1995-JP1933 | 19950925 |
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| RW: KE, MM, SD, SZ, UG, AT, BE, CH, DE, DK, ES, PR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BP, BJ, CP, CO, CI, CM, GA, GN, ML, MR, NS, SN, TD, TG | | | | |

JP 1994-231839 A 19940927

L7 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
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AU 9535341 A1 19960419 AU 1995-35241 19950925

JP 1994-231839 JP 1994-231839 A 19940927

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R: AT, BE, CH, DE, DK, ES, PR, GB, GR, IE, IT, LI, LU, NL, PT, SE

JP 1994-231839 A 19940927

WO 1995-JP1933 W 19950925

OS MARPAT 125:115147

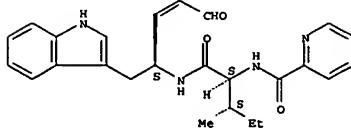
IT 178910-84-4P RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of peptide aldehyde derivs. as cysteine protease inhibitor and bone resorption inhibitor for treating bone diseases)

RN 178910-84-4 CAPLUS

CN 2-Pyridinocarboxamide, N-1-[(1-(1H-indol-3-ylmethyl)-4-oxo-2-butyl)amino]carbonyl-2-methylbutyl-, (1S-[1R*(R*),2R*])- (9CI) (CA INDEX NAME)

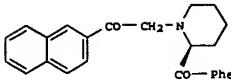
Absolute stereochemistry.
Double bond geometry unknown.



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L7 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
GI



I

AB I is the most potent synthetic multidrug resistance (MDR) modulator of a series of compds. and is equivalent in potency to FK506, however, it is a thousand-fold less potent than FK506 vs. PKBP inhibition. It is apparent that the structure component of the FK506 mol. that imparts functional immunosuppressive activity is not required for useful P-glycoprotein inhibition, since the synthetic PKBP inhibitors lack the structural element which impart functional activity.

AN 1995:84958 CAPLUS

DN 122:45705

TI Investigation of the effects of synthetic, non-cytotoxic immunophilin inhibitors on MDR

AU Hauske, James R.; Kajiji, Shama; Dorff, Peter; Julin, Susan; DiBrino, Joseph; Pailet, Simone

CS Central Research Division, Pfizer Inc., Groton, CT, 06340, USA

SO Bioorganic & Medicinal Chemistry Letters (1994), 4(17), 2097-102

CODEN: BMCLB8; ISSN: 0960-894X

DT Journal

LA English

IT 145021-58-5 145021-66-5 145021-67-6

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); BIOL (Biological study)
(synthetic noncytotoxic immunophilin inhibitors effect on multidrug resistance)

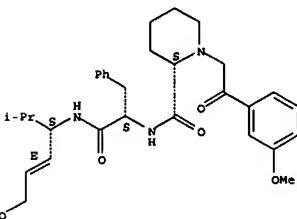
RN 145021-58-5 CAPLUS

CN 2-Piperidinocarboxamide, N-[2-[(4-(acetoxy)-1-(1-methylethyl)-2-butenyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-1-[2-(3-methoxyphenyl)-2-oxoethyl]-, [2S-[2R*[R*(1R*,2E*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

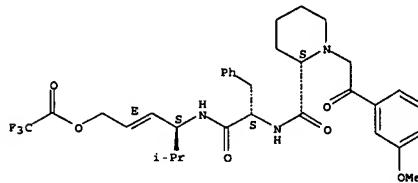
L7 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 145021-66-5 CAPLUS

CN Acetic acid, trifluoro-,
(2E,4S)-4-(((2S)-2-[[[2S]-1-[2-(3-methoxyphenyl)-2-oxoethyl]-2-piperidinyl]carbonyl]amino)-1-oxo-3-phenylpropyl]amino)-5-methyl-4-hexenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

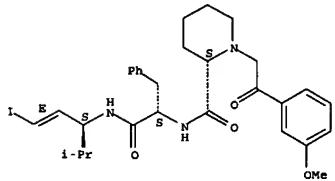


RN 145021-67-6 CAPLUS

CN 2-Piperidinocarboxamide, N-[(1S)-2-((1S,2E)-3-iodo-1-(1-methylethyl)-2-propenyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-1-[2-(3-methoxyphenyl)-2-oxoethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

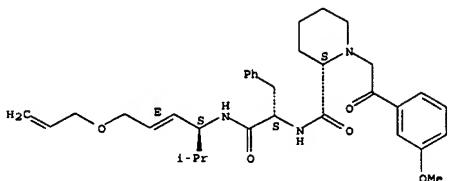
L7 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



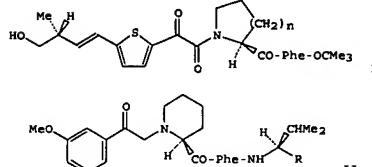
RN 145021-68-7 CAPLUS

CN 2-Piperidinocarboxamide, 1-[2-(3-methoxyphenyl)-2-oxoethyl]-N-[(1S)-2-((1S,2E)-1-(1-methylethyl)-4-(2-propenyl)-2-buteneyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
GI



AB Small mol.=FK-506 binding protein (PKBP) inhibitors, e.g.-I-(n = 1, 2) and II (R = CO-Phe-OMe, trans-CH:CHCH2O2CCP3, trans-CH:CHCH2O2CCF3) were prepared with inhibitory activity ranging from micromolar to nanomolar.

The design of these inhibitors derives from a structural anal. of the substrates for PKBP and cyclophilin. As a consequence of this anal. two key observations were made, namely: (1) amineketone moieties are suitable as PKBP recognition elements at the P1-P12 site, and (2) the P32-P42 site will accept a trans-olefin as a suitable mimetic of a peptide moiety.

The preparation of these nonpeptide inhibitors is readily accomplished by a protocol which includes the synthesis of chiral propargylic amines and their subsequent conversion into vinyl zirconium reagents.

AN 1993:22591 CAPLUS

DN 118:22591

TI Design and synthesis of novel PKBP inhibitors
AU Hauske, James R.; Dorff, Peter; Julin, Susan; DiBrino, Joseph; Spencer, Robin; Williams, Rebecca

CS Cent. Res., Div. Pfizer Inc., Groton, CT, 06340, USA
SO Journal of Medicinal Chemistry (1993), 35(23), 4284-96

CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

IT 145021-57-4P 145021-58-5P 145021-59-6P

145021-60-9P 145021-61-0P 145021-62-1P

145021-63-2P 145021-64-3P 145021-65-4P

145021-66-5P 145022-67-6P 145021-68-7P

145108-13-0P 145108-14-1P 145108-15-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and PK-506 binding protein inhibitory activity of)

RN 145021-57-4 CAPLUS

CN 2-Hexenoic acid, 4-[[1-[[1-[(2-(3-methoxyphenyl)-2-oxoethyl)-2-piperidinyl]carbonyl]amino]-1-oxo-3-phenylpropyl]amino]-5-methyl-, ethyl ester, [2S-[2R*[R*(2E,4R*)]]]- (9CI) (CA INDEX NAME)

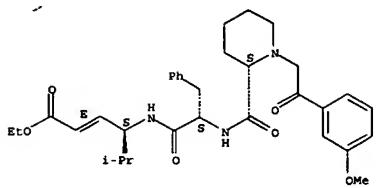
Absolute stereochemistry.
Double bond geometry as shown.

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L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

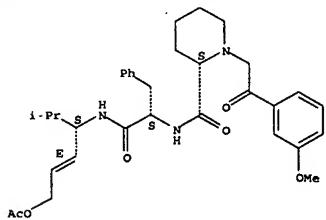
(Continued)



RN 145021-58-5 CAPLUS

CN 2-Piperidinecarboxamide, N-[2-[(4-(acetoxy)-1-(1-methylethyl)-2-butenyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-1-[2-(3-methoxyphenyl)-2-oxoethyl]-, [2S-[2R*(1R*,2E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



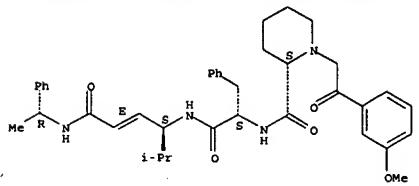
RN 145021-59-6 CAPLUS

CN 2-Piperidinecarboxamide, N-[2-[(4-(acetoxy)-1-(1-methylethyl)-2-butenyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-1-[2-(2-naphthalenyl)-2-oxoethyl]-, [2S-[2R*(1R*,2E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

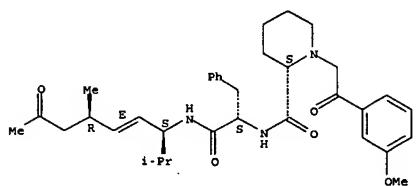
(Continued)



RN 145021-62-1 CAPLUS

CN 2-Piperidinecarboxamide, 1-[2-(3-methoxyphenyl)-2-oxoethyl]-N-[2-[(4-methyl-1-(1-methylethyl)-6-oxo-2-heptenyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-, [2S-[2R*(1R*,2E,4S)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



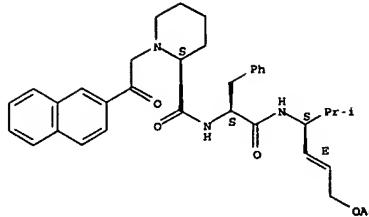
RN 145021-63-2 CAPLUS

CN 2-Piperidinecarboxamide, 1-[2-(3-methoxyphenyl)-2-oxoethyl]-N-[2-[(1-(1-methylethyl)-3-(3-oxocyclopentyl)-2-propenyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-, [2S-[2R*(1R*,2E,3(S))]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

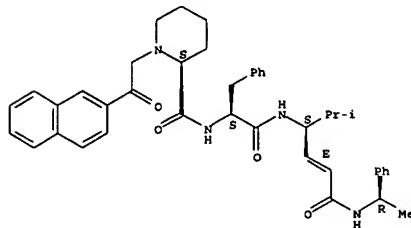
(Continued)



RN 145021-60-9 CAPLUS

CN 2-Piperidinecarboxamide, N-[2-[(1-(1-methylethyl)-4-oxo-4-(1-phenylethyl)amino)-2-butene-1-(phenylmethyl)ethyl]-1-[2-(2-naphthalenyl)-2-oxoethyl]-, [2S-[2R*(1R*,2E,4(S*))]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



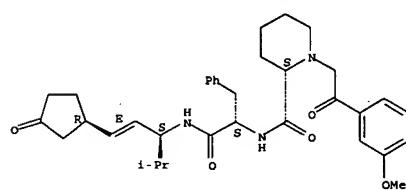
RN 145021-61-0 CAPLUS

CN 2-Piperidinecarboxamide, 1-(2-(3-methoxyphenyl)-2-oxoethyl)-N-[2-[(1-(1-methylethyl)-4-oxo-4-(1-phenylethyl)amino)-2-butene-1-(phenylmethyl)ethyl]-, [2S-[2R*(1R*,2E,4(S*))]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

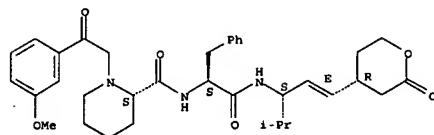
(Continued)



RN 145021-64-3 CAPLUS

CN 2-Piperidinecarboxamide, 1-[2-(3-methoxyphenyl)-2-oxoethyl]-N-[2-[(1-(1-methylethyl)-3-(tetrahydro-2-oxo-2H-pyran-4-yl)-2-propenyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-, [2S-[2R*(1R*,2E,3(S*))]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 145021-65-4 CAPLUS

CN 2-Piperidinecarboxamide, N-[(1S)-2-[(1S,2E)-4-(benzoyloxy)-1-(1-methylethyl)-2-butene-1-(phenylmethyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-1-[2-(3-methoxyphenyl)-2-oxoethyl]-, (2S)- (9CI) (CA INDEX NAME)

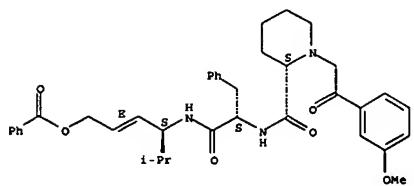
Absolute stereochemistry.
Double bond geometry as shown.

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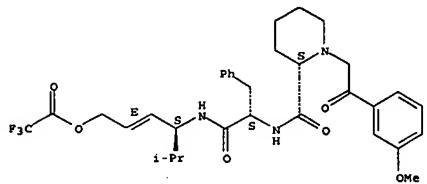
L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

(Continued)



RN 145021-66-5 CAPLUS
CN Acetic acid, trifluoro-, (2E,4S)-4-[(2S)-2-[(2-(3-methoxyphenyl)-2-oxoethyl)-2-piperidinyl]carbonyl]amino)-1-oxo-3-phenylpropylamino)-5-methyl-hexenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

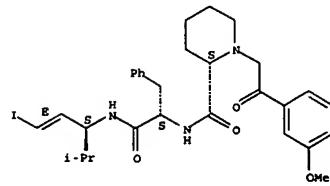


RN 145021-67-6 CAPLUS
CN 2-Piperidinecarboxamide, N-[(1S)-2-[(1S,2E)-3-iodo-1-(1-methylethyl)-2-propenyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

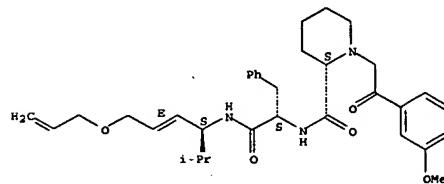
L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

(Continued)



RN 145021-68-7 CAPLUS
CN 2-Piperidinecarboxamide, 1-(2-(3-methoxyphenyl)-2-oxoethyl)-N-[(1S)-2-((1S,2E)-1-(1-methylethyl)-4-(2-propenyl)-2-buteneyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

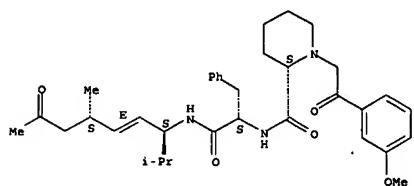


RN 145108-13-0 CAPLUS
CN 2-Piperidinecarboxamide, 1-[2-(3-methoxyphenyl)-2-oxoethyl]-N-[2-[(4-methyl-1-(1-methylethyl)-6-oxo-2-heptenyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-, [2S-[2R*[R*(1R*,2E,4R*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

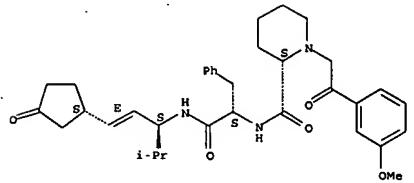
L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

(Continued)



RN 145108-14-1 CAPLUS
CN 2-Piperidinecarboxamide, 1-[2-(3-methoxyphenyl)-2-oxoethyl]-N-[2-[(1-(1-methylethyl)-3-(3-oxocyclopentyl)-2-propenyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-, [2S-[2R*[R*(1R*,2E,3(R*))]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

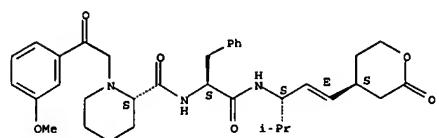


RN 145108-15-2 CAPLUS
CN 2-Piperidinecarboxamide, 1-[2-(3-methoxyphenyl)-2-oxoethyl]-N-[2-[(1-(1-methylethyl)-3-(tetrahydro-2-oxo-2H-pyran-4-yl)-2-propenyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-, [2S-[2R*[R*(1R*,2E,3(R*))]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

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COST IN U.S. DOLLARS

| | SINCE FILE ENTRY | TOTAL SESSION |
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